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MEDICAL PROCEEDINGS
MEDIESE BYDRAES

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'n Suid-Afrikaanse Tydskrif vir die Bevordering van die Geneeskunde

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IN THIS ISSUE · IN HIERDIE UITGAWE

Fellowship of the College of Surgeons of South Africa

The first Primary Examination for the Fellowship of the College of Surgeons of South Africa will be held on 30 September and 2—3 October 1957.

All those interested in this examination, who desire further information, may receive copies of the regulations on application to: Dr. T. B. McMurray, *Honorary Registrar*, P.O. Box 120, Cape Town.

Fellowship of the College of Physicians of South Africa

The first examination for the Fellowship of the College of Physicians of South Africa will be held in the first week of October 1957.

All those interested in this examination, who desire further information, may receive copies of the regulations on application to: Dr. T. B. McMurray, *Honorary Registrar*, P O. Box 120, Cape Town

Genootskap van die Kollege van Chirurge van Suid-Afrika

Die eerste Primêre Eksamen vir die Genootskap van die Kollege van Chirurge van Suid-Afrika word op 30 September en 2 en 3 Oktober 1957 gehou. Almal wat belangstel in hierdie eksamen en nadere inligting verlang, kan eksemplare van die regulasies ontvang as hulle aansoek doen by dr. T. B. McMurray, *Ere-Registrateur*, Posbus 120, Kaapstad.

Genootskap van die Kollege van Interniste van Suid-Afrika

Die eerste eksamen vir die Genootskap van die Kollege van Interniste van Suid-Afrika word gedurende die eerste week in Oktober gehou. Almal wat belangstel in hierdie eksamen en nadere inligting verlang, kan eksemplare van die regulasies ontvang as hulle aansoek doen by dr. T. B. McMurray, *Ere-Registrateur*, Posbus 120, Kaapstad.

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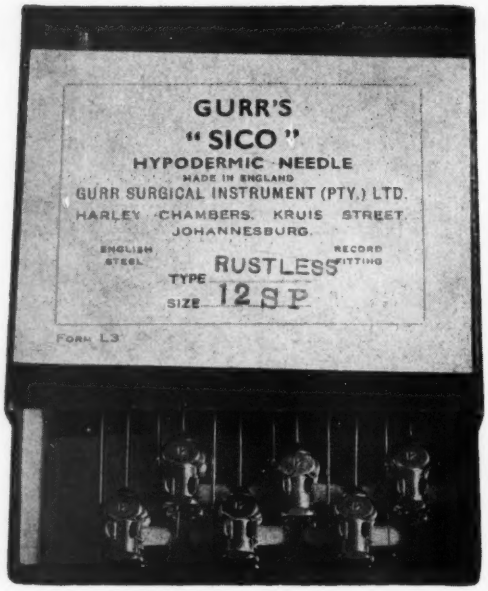

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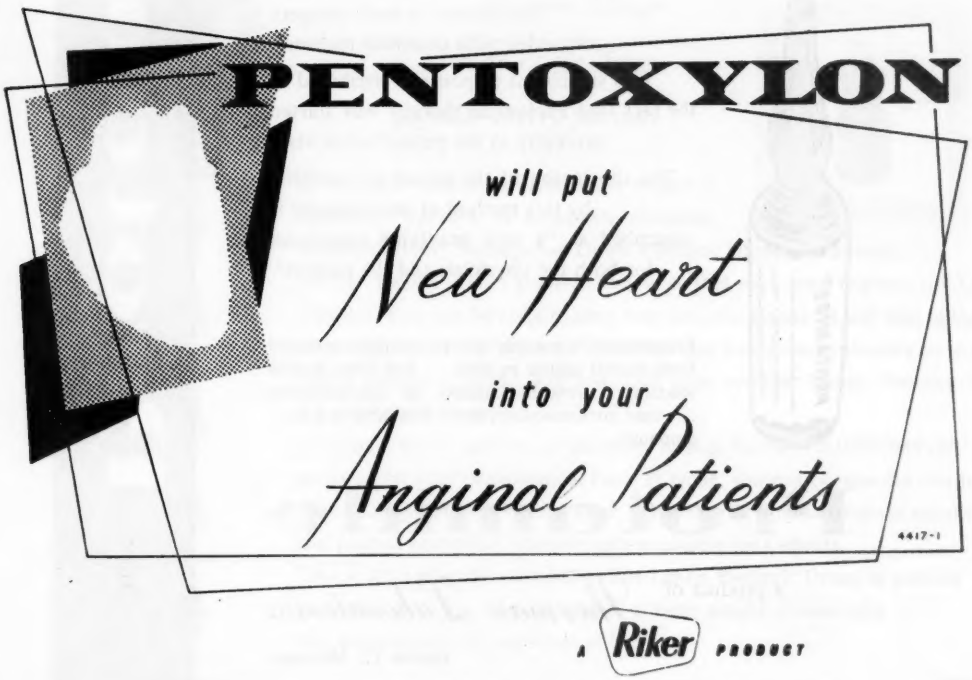

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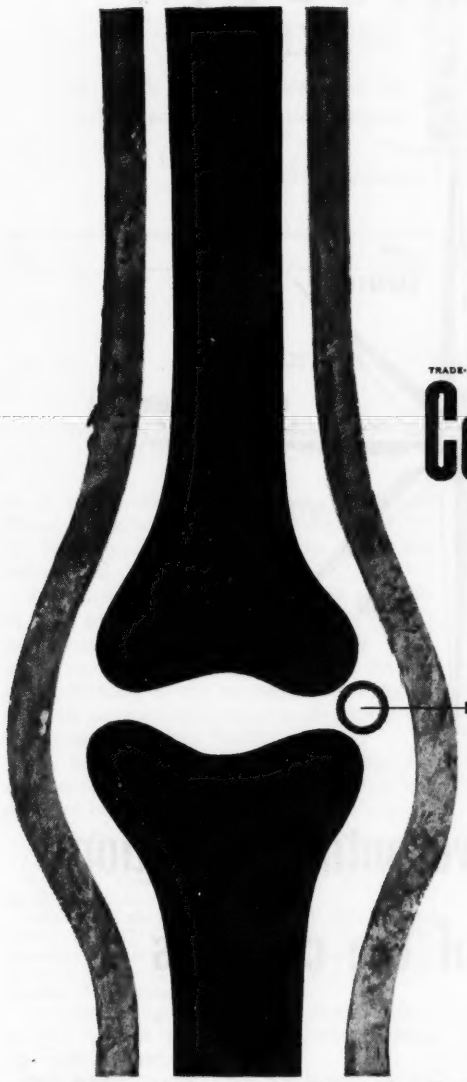

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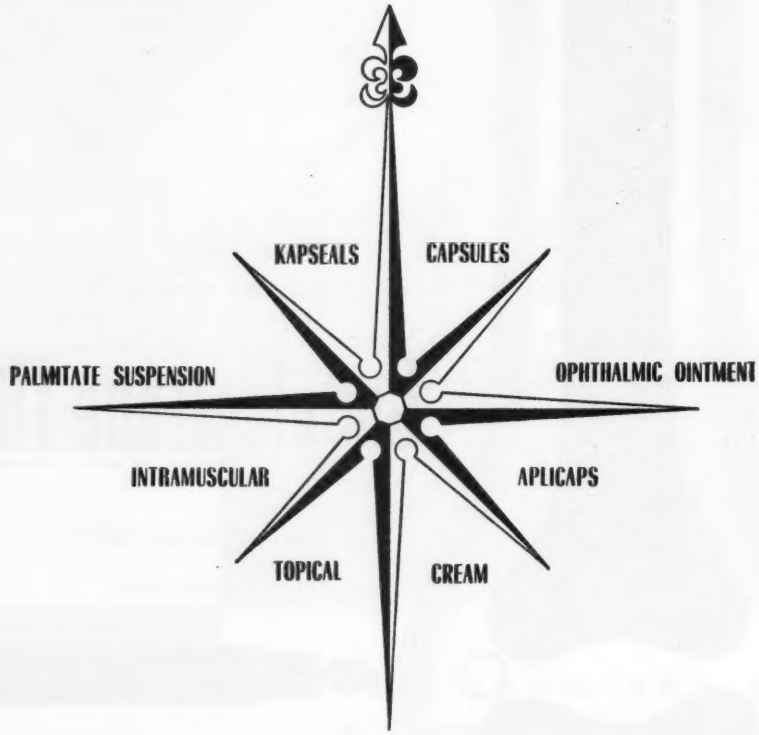

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Vol. 3 | 11 May 1957 Mei 11 | No. 10

EDITORIAL · REDAKSIONEEL

THE NUTRITION SOCIETY OF SOUTHERN AFRICA

At a memorable meeting held at Medical House, Johannesburg, on 11 February 1957, the Nutrition Society of Southern Africa was inaugurated.

The Society exists to advance the scientific study of nutrition and its membership is open to any suitably qualified person whose work, in the opinion of the Council of the Society, may contribute to the scientific knowledge of nutrition or to its application to the promorion of human and animal health.

The honour of being the first President was appropriately awarded to Dr. F. W. Fox, the doyen of nutrition research in South Africa.

The following officers were elected:

Chairman: Prof. J. T. Irving (Johannesburg).
Honorary Secretary and Treasurer: Dr. J. M. Latsky (Pretoria).
Members of the Council: Prof. J. F. Brock (Cape Town); Prof. D. G. Haylett (Pretoria); Dr. A. W. Lategan (Pretoria); Dr. W. A. Odendaal (Pretoria) *alternate*, Prof. S. L. Kark (Durban); and Dr. M. M. Suzman (Johannesburg).

At the inaugural meeting, three distinguished visitors to the Union were elected Honorary Members, viz.:

Prof. Martha Trulson, Chief Nutritionist, Department of Nutrition, Harvard University, Boston;
Prof. D. M. Hegstedt, Department of Biochemistry, Harvard University, Boston;
Prof. J. Gordon, Professor of Epidemiology, Harvard University, Boston.

These three well-known nutrition research workers are on a visit to South Africa at the

DIE VOEDINGSVERENIGING VAN SUIDELIKE AFRIKA

Op 'n gedenkwaardige vergadering wat op 11 Februarie 1957 in Mediese Gebou, Johannesburg, gehou is, is die Voedingsvereniging van Suidelike Afrika van stapel gestuur.

Die Vereniging is in die lewe geroep om die wetenskaplike bestuderings van voeding te bevorder, en lidmaatskap is oop vir enige geskikte gekwalifiseerde persoon wie se werk, volgens die mening van die Raad van die Vereniging, 'n bydrae kan lewer tot die wetenskaplike kennis van voeding, of die toepassing van daardie kennis op die bevordering van gesondheid by mense of diere.

Die eer om tot eerste president verkies te word, is met reg toegeken aan dr. F. W. Fox, doyen op die gebied van voedingsnavorsing in Suid-Afrika.

Die volgende ampsdraers is verkies:

Voorsitter: Prof. J. T. Irving (Johannesburg).
Ere-Sekretaris en Tesourier: Dr. J. M. Latsky (Pretoria).
Lede van die Raad: Prof. J. F. Brock (Kaapstad); Prof. D. G. Haylett (Pretoria); Dr. A. M. Lategan (Pretoria); Dr. W. A. Odendaal (Pretoria) *plaasvervanger*, Prof. S. L. Kark (Durban); en Dr. M. M. Suzman (Johannesburg).

Drie gedistingeerde besoekers aan die Unie is op die eerste vergadering tot ere-lede verkies, nl.:

Prof. Martha Trulson, Hoofvoedingsdeskundige, Voedingsdepartement, Harvard-universiteit, Boston;
Prof. D. M. Hegstedt, Departement van Biochemie, Harvard-universiteit, Boston;
Prof. J. Gordon, Professor van Epidemiologie,

invitation of the Ernest Oppenheimer Cardiovascular Research Unit, details of which were published in this Journal in December 1955, p. 214.

Those interested in the new Society and wishing to become members, should communicate with Dr. J. M. Latsky, Union Health Department, Pretoria. There is an entrance fee of 10/- and an annual subscription of 10/-.

Harvard-universiteit, Boston.

Hierdie drie bekende navorsingswerkers op die gebied van voedingsprobleme het na Suid-Afrika gekom op uitnodiging van die Kardiovaskulêre Navorsingseenheid Ernest Oppenheimer. Besonderhede oor hierdie eenheid is in Desember 1955 (bl. 214) in hierdie Tydskrif gepubliseer.

Diegene wat belang in die nuwe Vereniging stel en lede wil word, moet in verbinding tree met Dr. J. M. Latsky, Unie-departement van Gesondheid, Pretoria. Daar is 'n intreegeld van 10/-, en 'n jaarlikse subskripsie ook van 10/-.

METATARSUS PRIMUS VARUS AND HALLUX VALGUS DEFORMITY

L. H. MULLER, M.B. CH.B.

Department of Orthopaedics, Pretoria General Hospital, Pretoria

At least 60 different operations have been described to correct hallux valgus deformity.[1, 4] Of these about 14 are directed at the cause of the condition and are designed to correct the metatarsus primus varus deformity, with or without correction of the deviation of the great toe.

As it is the aim of this group of operations to reduce the angle between the first and second metatarsal permanently, it is pertinent to enquire whether the operation succeeds in this aim, and if the eventual functional result is satisfactory.

With this object in mind an unselected group of patients was examined who had undergone operative treatment for hallux valgus and metatarsus primus varus deformity at the Pretoria Orthopaedic Hospital. A large number of patients is treated annually, and as the same type of operation is employed routinely, it is possible to evaluate the final results.

THE OPERATION

No claim for originality is made, as the operation is essentially a combination of the methods described by McBride[3] and Joplin.[2]

It is confined to patients with hallux valgus bunion and metatarsus primus varus deformity, in whom no evidence of degenerative change in the first metatarso-phalangeal joint or other foot joints can be demonstrated.

The incision, which is made medial to the extensor of the great toe, begins just distal to the first metatarso-phalangeal joint and extends proximally for 3 inches. The subcutaneous tissue and the fascia are incised in the line of the skin incision, and the metatarso-phalangeal joint is exposed. While an assistant flexes the big toe and pushes up the head of the first metatarsal, a flap is dissected downwards

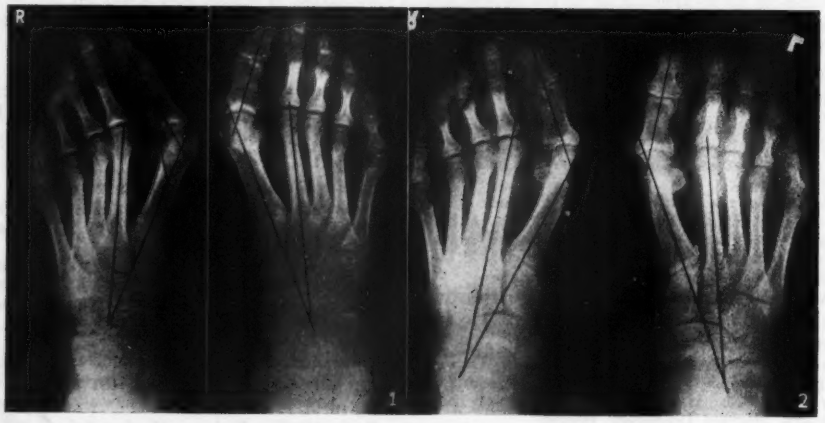

Fig. 1. Pre-operative radiograph showing the method of measuring the intermetatarsal and hallux valgus angles.
Fig. 2. Post-operative radiograph of the same patient. Hallux valgus improved, but no difference in the intermetatarsal angle.

exposing the exostosis over the medial aspect of the metatarsal head. This is removed through the vertical groove in the articular cartilage, indicating the non-functioning portion of the metatarsal head. The extensor of the big toe is now retracted medially, taking great care not to damage the tendon and the tissue overlying it, and the adductor hallucis is exposed in the first intermetatarsal space. The tendon is freed from its insertion into the base of the proximal phalanx of the big toe, and carefully dissected loose from the lateral sesamoid. The free end of the tendon is pulled through a hole drilled in the neck of the first metatarsal and, while an assistant approximates the first metatarsal to the second, it is sutured under tension to the tissue overlying the medial aspect of the metatarsal head. The wound is closed in layers and a plaster boot is applied with the object of keeping the first metatarsal in the adducted position. After 3 weeks the plaster is removed, gradual walking is allowed, and physiotherapy is instituted.

THE METHOD OF EXAMINATION

Since January 1953, 83 patients have undergone this operation. Some of the earlier cases could not be traced, and in others the pre-operative radiographs and clinical notes were incomplete. This left 28 cases and a total of 56 feet operated upon for final analysis, and clearly in no way distracted from the experience gained in examining the rest of the cases.

To assess whether the operation succeeded in reducing the metatarsus primus varus, and restoring the hallux valgus deformity, careful measurements of the angle between the first and second metatarsal and of the degree of hallux valgus were taken in the pre-operative radiographs (Fig. 1). These measurements were repeated in the post-operative radiographs (Fig. 2). All the radiographs were taken with the patients in the standing position. The results of these measurements, and the age and the sex of the patients are set out in Table I.

The subjective functional results set out in Table II were based on the following criteria.

TABLE I

Case	*Age*	*Degrees of Metatarsus Primus Varus*				*Degrees of Hallux Valgus*			
		Pre-Operative		*Post-Operative*		*Pre-Operative*		*Post-Operative*	
		Left	*Right*	*Left*	*Right*	*Left*	*Right*	*Left*	*Right*
1. E. V. T.	26	16	18	16	16	139	127	148	134
2. H. C. S.	28	13	12	13	13	133	136	136	140
3. A. J. M.	20	16	17	16	16	151	146	155	152
4. M. E. vV.	39	20	20	19	18	137	140	146	148
5. S. C. B. V.	17	12	13	12	12	156	158	158	160
6. M. M. vD.	17	11	10	10	10	152	154	155	157
7. W. J. V.	26	17	16	16	15	143	141	150	149
8. J. S. V.	37	14	16	15	16	142	140	150	148
9. C. S.	26	12	13	12	12	145	139	152	147
10. L. A. V.	17	14	14	13	12	143	142	151	150
11. C. B.	42	14	13	13	13	133	143	140	148
12. M. C. B.	31	12	11	11	11	148	158	151	153
13. E. B.	21	13	14	12	14	143	142	149	147
14. P. G.	18	10	11	9	8	155	154	158	156
15. M. H.	27	13	13	12	13	144	142	153	151
16. L. S. L.	16	16	14	14	14	143	145	150	152
17. C. V.	11	12	12	11	12	157	158	162	163
18. N. J.	18	11	14	12	12	150	142	152	152
19. S. E. P.	35	13	15	14	14	141	143	149	152
20. J. V.	35	15	14	15	14	145	147	154	154
21. A. M. vV.	21	13	12	12	12	148	150	155	157
22. M. E. B.	18	14	15	15	15	147	146	156	154
23. D. J. B.	22	15	15	15	14	150	149	155	155
24. F. de G.	34	12	14	13	13	152	153	156	157
25. P. J. J.	34	18	17	16	17	138	140	148	151
26. A. S. M.	23	13	14	13	13	148	147	154	156
27. H. E. M.	25	17	17	16	17	141	140	150	150
28. I. J. B. E.	39	14	13	14	14	145	146	153	155

*All the patients were females except for Cases 9 and 23.

TABLE II

Case	Subjective Functional Results.		
	Grade of Relief of Pain	Cosmetic expectations	Anaestbesia of toe
1	I	I	Slight
2	I	I	None
3	II	I	None
4	I	I	Slight
5	II	I	Yes
6	I	I	Yes
7	I	I	Slight
8	I	I	Slight
9	II	I	None
10	I	I	None
11	I	I	None
12	III	I	Yes
13	I	I	None
14	I	I	None
15	I	I	None
16	I	I	Slight
17	I	I	None
18	I	I	None
19	I	I	None
20	I	I	None
21	III	I	Yes
22	II	I	Yes
23	I	I	None
24	I	I	Slight
25	I	I	None
26	I	I	None
27	I	I	None
28	I	I	None
29	I	I	None

TABLE III

Case	Grade of Function of M.P Joint		Preservation of Toe Leverage
	Dorsiflexion	Plantar Flexion	
1	Slight limitation	More than 15°	Yes
2	More than 30°	More than 15°	Yes
3	Slight limitation	More than 15°	Yes
4	More than 30°	More than 15°	Yes
5	Slight limitation	More than 15°	Yes
6	More than 30°	More than 15°	Yes
7	More than 30°	More than 15°	Yes
8	More than 30°	More than 15°	Yes
8	More than 30°	More than 15°	Yes
9	More than 30°	More than 15°	Yes
10	More than 30°	More than 15°	Yes
11	More than 30°	More than 15°	Yes
12	Marked limitation	Marked limitation	No
13	More than 30°	More than 15°	Yes
14	More than 30°	More than 15°	Yes
15	More than 30°	More than 15°	Yes
16	More than 30°	More than 15°	Yes
17	More than 30°	More than 15°	Yes
18	More than 30°	More than 15°	Yes
19	More than 30°	More than 15°	Yes
20	More than 30°	More than 15°	Yes
21	Marked limitation	Marked limitation	Yes
22	More than 30°	More than 15°	Yes
23	More than 30°	More than 15°	Yes
24	More than 30°	More than 15°	Yes
25	More than 30°	More than 15°	Yes
26	More than 30°	More than 15°	Yes
27	More than 30°	More than 15°	Yes
28	More than 30°	More than 15°	Yes
29	More than 30°	More than 15°	Yes

A. *Grade of Relief of Pain.*
Grade
I. Complete relief of pain. Resumption of normal activity.
II. Occasional symptoms, causing no restriction of normal activity.
III. Intermittent limitation of normal activity.
IV. Total limitation of normal activity.

B. *Cosmetic Expectations.*
Grade
1. Satisfied with appearance of foot.
II. Dissatisfied with appearance of foot.

C. *Anaesthesia of the Big Toe.*

The objective function results, based on the degree of function of the metatarso-phalangeal joint and the preservation of the toe leverage, are set out in Table III.

DISCUSSION

The marked female preponderance in this series emphasizes the role of abnormal footwear in the etiology of the condition, especially in the bunion formation.

The results in Table I show that the intermetatarsal angles varied from 10-20 degrees. If experimental errors, allowing for mistakes of 1-2 degrees in the measurements, are taken into consideration, the results show that the metatarsus primus varus deformity was not corrected in a single instance. The hallux valgus deformity, however, was improved in all the cases.

This would seem to indicate that the elaborate method of securing the adductor hallucis to the neck of the first metatarsal is not justified, and that its prime object is to release the deforming effect on the proximal phalanx. The general impression was gained, however, that the fixation of the adductor hallucis to the neck of the first metatarsal does give stability to the metatarsal itself, which helps to maintain a normal long arch of the foot.

The subjective functional results show that all the patients were satisfied with the appearance of their feet. This is important because, apart from relief of pain, the patient at least expects his feet to appear more normal after the operation, and naturally wants to wear narrower shoes. Most of the patients had no restriction of normal activity.

A large number of patients complained of slight or marked anaesthesia of the big toe,

indicating that the nerve to the medial side of the big toe is frequently injured.

Limitation of movements at the first metatarso-phalangeal joint occurred quite frequently. This may be due to damage of the extensor hallucis during the operation or to fibrosis as a result of the method of fixation of the adductor hallucis to the lateral joint capsule.

Although this type of operation does not seem to improve the metatarsus primus varus deformity, the short period of post-operative immobilization offers a distinct advantage over the prolonged period of disuse that follows after any of the various osteotomies that have been recommended.

SUMMARY

A type of operation employed at the Pretoria Orthopaedic Hospital for the correction of metartarsus primus varus and hallux valgus bunion deformity is described.

An analysis of the results is set out in tabular form and the findings discussed.

OPSOMMING

'n Operasie wat gebruik word by die Ortopediese Departement van die Pretoriase Algemene Hospitaal vir die herstel van metatarsus primus varus en hallux valgus deformiteit word beskryf.

'n Ontleding van die resultate word uiteengesit in die vorm van tabelle, en die bevindings word bespreek.

I wish to express my thanks to Mr. J. G. du Toit for his encouragement and for the interest he has taken.

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CARDIAC OUTPUT

CHANGING VIEWPOINTS ON ITS REGULATION

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Much work during the past 50 years has been devoted to the regulation of the output of the heart, probably the most difficult and controversial subject in cardiology to-day. An understanding of the mechanisms involved is important not only in the physiology of the normal circulation, but also in such pathological states as congestive heart failure, shock, valvular disease, etc. It is unlikely that the clinical manifestations of these conditions will be properly understood until we know more about the basic problem of cardiac output itself.

Many of the difficulties encountered in this field result from a too ready application of results obtained in the laboratory to normal, intact human beings. Much information can be obtained from an active and critical study of the living patient. For this reason, an up-to-date knowledge of current work in this field is by no means academic for the general practitioner, whose role is to-day increasingly important.

The cardiac output (minute volume) is the quantity of blood pumped out by the heart each minute. This is equal to the quantity ejected with each heart beat (stroke volume) multiplied by the number of beats per minute. Changes in cardiac output may therefore be brought about by changes in either the stroke volume or the heart rate, or both. For the purposes of this discussion, it is immaterial whether one considers the left or the right side of the heart, as (over any appreciable interval of time) the outputs of the left and right ventricles must be equal.

CLASSICAL CONCEPTS

The classical concepts of the regulation of cardiac output, especially with regard to stroke volume, date from the second half of the nineteenth, and the early part of the twentieth century. Starling,[27] reviewing his own work and that of his predecessors, in 1915 formulated his *Law of the Heart* as follows:

'The law of the heart is thus the same as the law of muscular tissue generally, that the energy of contraction, however measured, is a function of the length of the muscle fibre.'

He had also described it[19] by stating:

'The output of the heart is a function of its

filling; the energy of its contraction depends on the state of dilatation of the heart cavities.'

Despite the fact that Starling's law refers to fibre length, or diastolic volume, the assumption is often made that diastolic volume is largely determined by the effective venous filling pressure,[25] and hence the form in which Starling's law is usually understood has been typically described by McMichael[14] as follows:

'Starling showed that the main factor determining the output of the heart was the venous filling pressure. The filling pressure determines the diastolic length of the myocardial fibres, which in turn determines the strength of the subsequent systolic contraction. . . . When the auricular pressure is raised, the output increases and, conversely, lowering the right auricular pressure reduces the output.'

There is abundant evidence in the literature that in the experimentally controlled or isolated heart, with constant heart rate and blood pressure, stroke volume and hence cardiac output are determined by the effective venous filling pressure.[25, 30] Starling's concepts were widely accepted by both physiologists and clinicians, and were assumed to be directly applicable to human beings. They appeared to provide an explanation for many findings in patients with both normal and diseased hearts. Most physiology textbooks, and the teaching in medical schools to-day, continue to emphasize the findings in the isolated heart, heart-lung and other experimental preparations, and imply, even if they do not specifically say so, that these laws govern the circulation under normal conditions.

There is a large body of evidence which questions whether cardiac output is actually determined by venous pressure in the intact, human circulation. While some of this evidence appears to support the applicability of Starling's law, there is much that does not, and it is therefore necessary to review this evidence.

Stead and Warren[28] have shown that the cardiac output at rest is increased in anaemia, thyrotoxicosis, arteriovenous aneurysms and anxiety states, without any increase in venous (right atrial) pressure, unless failure is present; that drugs such as paradrenal and angiotonin raise right atrial pressure without increasing cardiac output, while tetraethylammonium bromide causes a sharp fall in right atrial pressure with a rise in cardiac output; and finally, that the first effects of adrenaline given intravenously in small doses is to raise cardiac output with either no change or a slight drop in right atrial pressure. On opening and closing arterio-venous aneurysms[17] and areas of reactive hyperaemia[28] by means of pneumatic cuffs, marked and almost instantaneous changes in cardiac output were observed without consistent alteration in right atrial pressure. Rapid alterations in right atrial pressure induced by bleeding or venous infusions resulted in no consistent changes in output.[29] In exercise, too, no direct relationship has been found between cardiac output and effective venous pressure.[2] Numerous other workers[1, 3, 5, 7, 9, 11, 12, 24, 26] have failed to demonstrate a relationship between cardiac output and effective venous pressure under a variety of conditions.

It is only in the isolated heart, heart-lung and other experimental preparations,[10, 25, 28] in conditions with low blood volume, such as shock[15, 28] and in congestive heart failure,[14, 21] that right atrial or effective venous pressure appears to be an important factor in determining variations in cardiac output. Similar conclusions were reached by Gregg *et al.*[8] as a result of their studies on anaesthetized open- and closed-chest dogs, and on normal unanaesthetized dogs. They found that as one more closely approached the normal state, the deviations from Starling's law became larger and more numerous. In the normal dog they found no direct relationship between left ventricular end-diastolic pressure (effective venous pressure), stroke volume and stroke work.

Stead and Warren[28] concluded that

'the output of the heart in the presence of an adequate volume of blood is varied by changes in ventricular relaxation and contraction which are independent of fairly wide variations in atrial pressure. The ventricles play an active rather than a passive role in determining the cardiac output.'

Since Starling's law has been found to operate only under strictly limited conditions, Rushmer[23] has proposed the following modification of Starling's law of the heart:

'The law of the *experimentally controlled heart* is the same as the law of skeletal muscle in a nerve-muscle preparation, namely the energy released during contraction is related to the initial length of the muscle fibres under equal states of responsiveness.' (Italics inserted.)

Rushmer[23] has recently redirected attention to the fact that most statements regarding the applicability of Starling's law, actually neither confirm nor deny it because they deal with the effective filling pressure of the ventricle, instead of the initial fibre length or diastolic volume. The law would only be confirmed if the diastolic volume of the ventricle was found to increase simultaneously with the increase in cardiac output found, for example, during exercise.

Several techniques have been used to deter-

mine changes in volume of the heart during the cardiac cycle. One is by X-rays of the heart,[2, 10, 18, 26] preferably in two planes at right angles to each other, and the calculation of areas and volumes during various stages of the cardiac cycle from the X-ray plates. Another is the estimation of the sizes of the separate ventricles in intact dogs by cine-fluorography following the direct injection of radio-opaque material into the ventricles.[24] A further technique has been the introduction of a gauge into the hearts of dogs, and when they have recovered from the operation, to record the changes in transverse diameter of the left ventricle under a variety of physiological conditions, such as sleeping, waking and exercise.[22]

With the X-ray technique, evidence has steadily been accumulating since 1902—and was well established even by 1938—that the changes in diastolic size of the heart with exercise *do not* conform to Starling's law, and in many cases are just the reverse of what might be expected.[10] The heart is always *larger* when resting in the recumbent position than it is during exercise.

As neither diastolic volume nor the effective venous filling pressure determines stroke volume and cardiac output in the intact heart, it is necessary to go back to first principles to understand the factors that are important.

CURRENT CONCEPTS

Stroke volume is determined by the capacity of the ventricle at the end of diastole (diastolic volume), less the residual volume of blood remaining in the ventricle at the height of systole, immediately before closure of the semilunar valves. According to the well-known *All-or-none Law of the Heart,* the heart contracts maximally, to the best of its ability, with each heart beat. This concept, orginating from work on the isolated frog ventricle,[20] has unconsciously misled many research workers, who as a result have neglected to consider the possibility that one of the ways in which the normal heart may control its stroke volume is *by altering the degree or extent of its contraction during systole.* That this is indeed the case has recently been demonstrated.[2, 22, 24]

It will thus be seen that cardiac output depends on changes taking place simultaneously in at least 3 variables: heart rate, diastolic volume of the ventricle and, especially, the degree of emptying during systole.

In addition to the foregoing, cardiac output is also influenced by such factors as the state of the myocardium and the coronary circulation; blood volume and its distribution; the concentrations of oxygen, carbon dioxide and the various metabolites and hormones in the circulating blood and myocardium; and (perhaps most important of all) the nervous system. However, all these factors produce their effects through alterations in the 3 variables already mentioned and are best studied in this way.

The changes taking place in heart rate, ventricular diastolic volume and degree of systolic emptying in various conditions such as change in posture, exercise, anaesthesia, etc., will now be examined. Fig. 1 synthesizes some of the evidence into a unified picture of the changes taking place. It should be noted, however, that the quantities indicated are hypothetical, as all the various factors are not usually recorded simultaneously in investigations of this kind.

Changes in posture alter the distribution of reserve blood and heart size. On lying down, there is a considerable shift of blood from the lower extremities to the thorax. This amounted to an average of 643 c.c. in one investigation,[26] and up to 800 c.c. in another.[2] Most of this reserve blood is accommodated in the lungs, especially in the pulmonary veins, with a smaller amount in both sides of the heart. Nylin[18] found that the diastolic volume of each ventricle in the lying position was about 171 c.c., that about 71 c.c. was ejected during each systole, leaving a residual volume of 100 c.c. in the ventricle at the end of systole.

On the change from lying to the standing position, much of the reserve blood leaves the heart and lungs, moving peripherally to the lower extremities. In the investigation quoted,[18] there was a reduction in diastolic volume from 171 to 90 c.c., stroke volume from 71 to 45 c.c. and residual volume from 100 to 45 c.c. The heart rate increases on standing up, but this is not sufficient to compensate for the diminution in stroke volume, and as a result there is a net decrease in cardiac output (Fig. 1). It should be noted that there is an increase in the *degree* of systolic emptying in the standing position.

These changes, occurring in the movement from the lying to the standing position, are probably brought about by changes in the autonomic nervous system, possibly induced by changes in blood distribution acting on receptors situated in the great veins and in

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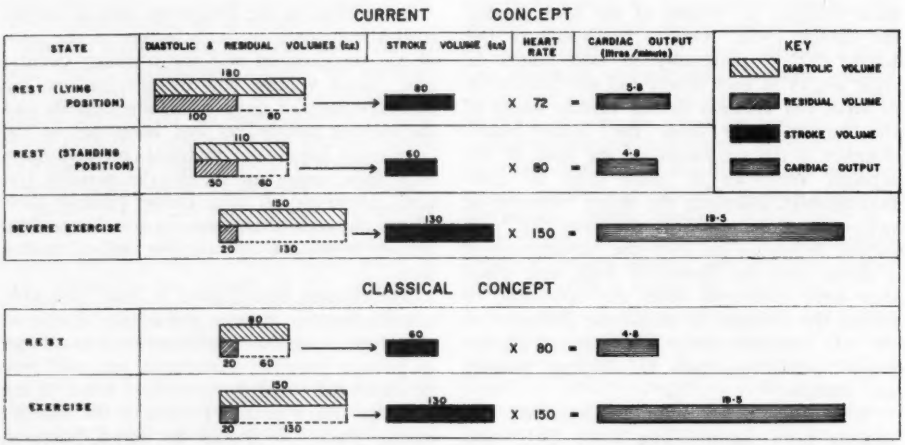

Fig. 1. The diagram indicates the changes taking place in diastolic volume, residual volume, stroke volume, heart rate and cardiac output under different conditions, according to current and classical concepts. (*Note:* The values given are hypothetical and do not apply to any particular investigation.)

the walls of the auricles and ventricles. These changes in autonomic regulation are such that, on lying down, the parasympathetic appears to predominate—with decrease in heart rate and an increase in the diastolic volume of the heart. There is a reduction in the degree of contraction of the ventricle, and the stroke volume, although increased, now forms a smaller proportion of the diastolic volume. On standing, the sympathetic apparently predominates—with increased heart rate, smaller diastolic size and a greater extent of contraction, albeit a smaller stroke volume than when in the lying position.[26]

It is well known that athletes usually have larger hearts and slower pulse rates than do untrained subjects, both in the standing and lying positions. Sjöstrand[26] has shown that the diastolic volume of the heart in the normal subject is very closely correlated with the total blood volume. The blood volume in athletes and persons in training is larger than in untrained individuals, and this probably accounts for their increased heart size. The bradycardia found in athletes is probably a manifestation of parasympathetic predominance induced by the increased blood volume acting on the stretch receptors mentioned. This vagal predominance may in addition account for the tendency of athletes to manifest the symptoms of vagotonia.[26]

Similarly, the reduction in heart size and the increase in heart rate found in cases with low blood volume, due to haemorrhage or dehydration, is probably the result of the change in blood volume inducing alterations in autonomic balance.

These findings may be put to clinical use by measuring the blood volumes of cases with enlarged hearts, but with no obvious signs of heart disease. A normal relationship between heart size and blood volume would in such cases tend to exclude a diagnosis of pathological enlargement of the heart.[13]

This relationship between heart volume and blood volume may also be operating in cases with congestive heart failure, although other factors probably predominate in these cases.

The increased cardiac output found during *exercise* has been intensively investigated.[2, 10, 23] This increase is achieved by increases in both heart rate and stroke volume. The chief factor producing the increase in stroke volume is the more complete emptying of the ventricle during systole, with reduction in the amount of residual blood. In some cases the diastolic volume of the ventricle is found to increase slightly with exercise (as in Fig. 1); in others it remains the same size or is a little smaller. However, *during exercise the diastolic volume is never as large as when the subject is resting in the lying position.* According to the Starling hypothesis (Fig. 1), the diastolic volume of the ventricle should be larger during exercise than at rest.

The extent to which the stroke volume may increase during exercise seems to depend mainly on the reserve blood volume available.

The increased reserve blood volume and increased diastolic ventricular size found in athletes enable them to increase their stroke volumes to a far greater extent than can untrained persons,[2] the latter achieving an increase in cardiac output chiefly by means of an increase in heart rate.

In one investigation[4] into the effects of exercise on untrained subjects in the lying position, it was found that most of the increased cardiac output was achieved by increase in heart rate, with only slight increase in stroke volume. In this study, however, heart volumes were not measured.

It has been suggested by Hamilton[9, 10] that the level of the cardiac output is regulated by the direct action of the nervous system (through a reflex arc with afferents arising in the stretch receptors of the aorta and carotid bodies) in such a way as to maintain arterial blood pressure at a relatively constant level in the face of changes in the state of dilatation or contraction of peripheral arterioles induced by exercise and other states. This is an attractive hypothesis. However, the mere anticipation of work increases cardiac output long before the suggested mechanism could come into operation. This indicates direct cortical control in these circumstances. Further, cutting off the circulation to exercising muscles by means of pneumatic cuffs produces no consistent lowering of cardiac output.[2] Cardiac output during moderate exercise has been shown by similar procedures[2] to bear no definite relationship to the level of oxygen consumption or to the effects of anaerobic metabolites, formed in the working muscles on the heart or nervous centres. It would be desirable, the authors point out, for this line of investigation to be pursued, especially at higher rates of exercise.

Anaesthesia induces profound changes in the circulation. It has been found that during anaesthesia there is a marked shift of reserve blood away from the heart and pulmonary circulation into the systemic circulation.[6, 26] As a result, heart size and diastolic volume decrease, and the heart has very little reserve blood with which to maintain cardiac output at normal levels. The cardiac output often declines,[6] in some cases to less than half of normal, without any warning drop in blood pressure.[16]

Opening the chest cavity during an operation has been found to produce a marked shrinkage in the size of the heart,[23] together with a profound drop in cardiac output.

These findings in anaesthetized and in thoracotomized subjects should make one very cautious about transferring data obtained under these conditions to intact unanaesthetized humans. The same argument applies even more forcefully to the results of experiments on anaesthetized animals.

CONCLUSIONS

The mechanism which determines the level of the output of the heart in the ***normal, intact, unanaesthetized subject*** has been discussed in the light of evidence from the literature.

The classical concepts, epitomized by Starling's law, are invalid for normal human or other animal subjects, in that cardiac output is related neither to the diastolic size of the ventricle nor to the effective venous filling pressure. Instead, it has been shown that the stroke volume is determined by the diastolic volume and the degree of emptying of the ventricle during systole, and that these (together with changes in heart rate) result in a particular level of cardiac output.

From all the evidence, it would seem that the 3 factors already mentioned, viz. heart rate, ventricular diastolic volume and degree of emptying during systole, are all under nervous control. It has been suggested that impulses arising reflexly from stretch receptors in the great veins and heart, centrally in the cortex, and from proprioceptors or chemoreceptors in the muscles during work, may be the main factors which regulate the cardiac output to the level required during muscular work and other physiological conditions.

More intensive investigations along these lines will, however, have to be done before the matter is settled.

SUMMARY

Starling's law of the heart has been shown to be applicable only in the experimentally controlled heart, in shock and in other abnormal conditions.

In the normal, intact, unanaesthetized subject, the cardiac output is controlled by nervous and other factors producing alterations in heart rate, ventricular diastolic volume and, especially, the degree of emptying of the ventricle during systole.

OPSOMMING

Die meganisme wat die peil van die vermoë van die hart van die ***normale, intakte, ongenarkotiseerde persoon*** bepaal, is bespreek in die lig van die getuienis wat aan leesstof ontleen is.

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Die klassieke begrippe, saamgevat in Starling se wet, geld nie vir normale menslike of ander dierlike voorwerpe nie, want die hartvermoë staan nie in verband òf met die diastoliese grootte van die hartkamer òf met die doeltreffende aderlike vullingsdruk nie. Inteendeel is daar aangetoon dat die slagvolume vasgestel word deur die diastoliese volume en die mate van ontlediging van die hartkamer tydens die saamtrekkingsfase, en dat hulle (saam met veranderings in die harttempo) 'n besonder peil van die hartvermoë tot gevolg het.

Aan die hand van al die getuienis skyn dit asof die reeds genoemde 3 faktore, nl. die harttempo, die diastoliese volume van die hartkamer en die mate van ontlediging tydens sistole, almal onder beheer van die senuwees staan. Daar is aan die hand gedoen dat impulse wat reflektories ontstaan uit rek-reseptore in die groot are en hart, sentraal in die cortex, en uit proprioseptore of chemoreseptore in die spiere tydens arbeid, bes moontlik die hooffaktore kan wees wat die hartvermoë reguleer tot die peil wat tydens spierarbeid of ander fisiologiese toestande nodig is.

Intensiewe ondersoek op hierdie gebied sal egter gedoen moet word voordat volkome helderheid oor die saak verkry is.

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VINCA ROSEA L. (LOCHNERA ROSEA REICHB.) AND THE TREATMENT OF DIABETES MELLITUS

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The plant *Vinca rosea,* belongs to the genus Vinca (Lochnera) and the family Apocynaceae.

The presence of alkaloids in several of the species of this genus has been reported, viz. in *V. lancea,*[3] *V. pubescens,*[4] *V. rosea,*[5] *V. major*[6] and *V. minor.*[4] The alkaloid isolated from *V. rosea* is known as vinceine.[5]

It is a widely held opinion amongst laymen in South Africa that the extract of *Vinca rosea* has curative properties in diabetes mellitus.

Some diabetic patients, therefore, do not hesitate to use this plant and often claim remarkably good results. This is in disparity with the results of different investigators.[1, 2]

The generally accepted procedure is to pour a cup of boiling water on to a dessertspoonful of dried semi-pulverized leaves of the plant. After 1-2 hours the extract is decanted and is ready for use. The recommended dosage is 1-2 teaspoonfuls 3 times a day.

Within the last few years, *Rauwolfia serpentina* and its alkaloids have come into prominence in the treatment of hypertension. It has also been shown that the basic ring structures of the alkaloids of various Apocynaceae such as Rauwolfia and Alstonia are essentially similar.[7] The importance of *V. rosea* as a potential source of related hypotensive alkaloids thus becomes apparent.

The alleged anti-diabetic activities of this plant, as well as its possible hypotensive action, therefore persuaded us to investigate the curative properties of the plant.

METHODS

1. *Preparation of* V. rosea *Extract and Powder.* In a preliminary experiment 200 c.c. of boiling water were poured on to 20 g. of the dried leaves of the plant. After 10 hours the leaves were filtered off. In preliminary tests with the infusion, it was noticed that the addition of 96% alcohol precipitated a fluffy substance. After drying, this substance has an off-white colour and can be combusted almost completely at a temperature of 300° C. Hardly any residue is left.

It was decided to investigate both the aqueous extract and the dried powder. This being our purpose, the extract and the powder were prepared in the following way: about 100 g. of the dried leaves were weighed off in a 2-litre flask, which was then filled with water at 80° C. This temperature was maintained for 18 hours. The leaves were next filtered off, and 96% alcohol was added to the filtrate in the ratio of 1 : 2. This mixture was then heated to near boiling point and allowed to cool slowly so that the substance[5] mentioned above, could precipitate.

The mixture of water and alcohol was then decanted; the whole process was repeated with 96% of alcohol, and the mixture was filtered through a Buchner funnel. The precipitate was then washed with 100-150 c.c. of 100% alcohol, followed by the same amount of ether so as to remove all the water. The filter paper with the precipitate was then carefully removed and dried on a sandbath: 100 g. of dried leaves furnished about 3.0 g. of dried powder.

2. *Trials on Animals.* Before this substance was tried out on diabetic patients, is was given a trial on normal young albino rats. Thirty rats were divided into 3 groups of 10 animals each; one group was treated with the extract, another group with the powder, and the third group served as control. After 7 weeks no difference between the different groups was noticed. The digestive tract, liver, kidneys, heart and lungs were examined, but neither macroscopic nor microscopic lesions could be found.

3. *Trials on Diabetic Patients.* The extract and the powder were next tried out on a few diabetic volunteers from the medical wards of the Pretoria General Hospital. The blood sugar level of 3 patients between the ages of 22 and 35 years was controlled in such a way by means of diet and insulin-therapy that the fasting blood sugar level ranged between 175 and 220 mg. per 100 c.c. With these levels. the urine developed a yellow to red colour with Benedict's reagent.

The dose of insulin was then reduced by 50% in each patient. The urine was tested every morning and evening with Benedict's qualitative sugar test, and the fasting blood sugar level was determined after 3 days. There was a more or less prompt rise in the blood sugar level, and after the second day the urine of all 3 patients developed an orange to red colour with Benedict's test. From the third day onwards the patients received, in addition to their insulin, one ounce of the plant extract 3 times a day. This treatment was continued for 6 days. The urine was tested as before, and the fasting blood sugar level was determined on the morning of the 6th and 9th days.

The *V. rosea* powder was then tried out on 5 patients in exactly the same way as the extract, except that each patient took 2 capsules (Parke, Davis No. I type) of the powder 3 times a day for 6 days, instead of the extract. In 3 of these patients the blood pressure was taken every morning and evening from the first day of the experiment.

RESULTS

Neither the aqueous nor the powder decreased the blood sugar level. In spite of the treatment, the blood sugar revealed a relatively slow but continuous rise. This was contrary to what we expected as a result of the qualitative urine tests. Judged on the qualitative urine tests alone, the diabetic condition improved and the degree of glycosuria decreased in 5 of the 8 patients after treatment with *V. rosea* extract

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and powder. In at least 5 of the 8 patients the Benedict test, therefore, did not reveal the true condition of the blood sugar (Tables I-III). The *V. rosea* material had no noticeable effect on the blood pressure.

TABLE I: POSITION BEFORE START OF EXPERIMENT

Patient No.	*Age*	*Insulin Dose*	*Fasting Blood Sugar Level (Mg. per 100c.c.)*	*Urine (Benedict's Test)*
1.	23	40	190	Yellow-green
2.	26	80	224	Red
3.	31	30	185	Yellow-green
4.	42	24	196	Greenish-yellow
5.	51	20	175	Blue-green

TABLE II: POSITION ON THE THIRD DAY AFTER A 50% REDUCTION IN INSULIN DOSAGE

Patient No.	*Age*	*Insulin Dose*	*Fasting Blood Sugar Level (Mg. per 100c.c.)*	*Urine (Benedict's Test)*
1.	23	20	255	Red
2.	26	40	310	Red
3.	31	15	235	Red
4.	42	12	216	Yellow
5.	51	10	194	Yellow-green

TABLE III: POSITION ON THE SIXTH DAY (THIRD DAY OF *V. rosea* SUBSTANCE + INSULIN

Patient No.	*Age*	*Insulin Dose*	*Fasting Blood Sugar Level (Mg. per 100c.c.)*	*Urine (Benedict's Test)*
1.	23	20	296	Orange to red
2.	26	40	335	Red
3.	30	15	250	Yellow
4.	42	12	228	Green-yellow
5.	51	10	201	Yellow-green

DISCUSSION

The results seem to indicate that neither the aqueous solution nor the *V. rosea* powder used in this investigation has any insulin activity, at least as far as the blood sugar is concerned. This is in agreement with the results of others.[5, 6, 8] According to Epstein[5] the plant has a weak digitalis action. Corkill and Doutch[6] prepared an extract from the leaf of the plant which they regarded as an ideal purgative in chronic constipation. These workers thought the benefit derived by diabetics from the plant was due probably to its weak digitalis and purgative action. This is most probably also the explanation for the claim of 2 of the patients that they felt better during the treatment with insulin + *V. rosea* material than with insulin alone.

There are indications that the plant substance had some effect on the glycosuria in 5 of the patients. One patient treated with the extract and 2 treated with the powder did not reveal this effect. Corkill and Doutch[6] also noticed an apparent diminution of the glycosuria in one of their patients and regarded it as an indirect effect.

The explanation for the discrepancy between the blood sugar levels and the qualitative urinary tests in the present work is not clear, but the following possibilities must be considered:

1. A rise in the renal threshold for glucose.
2. A stimulation of glucose reabsorption by the renal tubules.
3. A qualitative change in the excreted glucose.
4. Interference with the Benedict test by one or the other substance present in the plant and which is excreted in the urine.

Three patients, one treated with the extract and the other 2 treated with the powder, showed no discrepancy between blood sugar level and the qualitative Benedict test. One of these patients (No. 2), was 67 inches tall and weighed only 97 lb.

If a rise in the renal threshold for glucose is the explanation for the discrepancy between blood sugar level and urine tests, one would perhaps expect higher blood sugar levels. This is, however, not necessary, if we regard the raised blood sugar level of diabetics as an effort on the part of the body to compensate for an insulin deficiency. According to this view one of the main functions of insulin is to make it possible for the tissues to use glucose at a lower blood sugar level.

The blood pressures of the 3 patients who were regularly checked were not significantly altered by the plant preparation. The pressures of these patients were, however, within physiological limits before the start of the experiment. The latter fact, as well as the small number of cases used, does not justify any definite conclusions.

SUMMARY

An extract and a powder were prepared from *Vinca rosea* and tried out first on animals (to test for any toxicity) and then on 8 diabetic patients.

There were no indications that the plant substance had any insulin-like activity on the blood sugar level.

The qualitative Benedict test for glycosuria was, however, affected in 5 of the patients.

OPSOMMING

'n Ekstrak en 'n poeier is berei vanaf die plant, *Vinca rosea*, en is eers op diere uitgetoets (vir enige

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toksisiteit) en daarna op 8 diabetiese pasiënte.

Daar is geen aanduiding dat die plant 'n insulienagtige uitwerking het op die bloedsuikerkonsentrasie nie.

Dit is egter wel moontlik dat die graad van glukosurie by 5 van die pasiënte beïnvloed is.

This investigation has been made possible by a grant received by one of us (B. J. M.) from the Council for Industrial and Scientific Research.

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NOTES AND NEWS · BERIGTE

POLIO FANTASIES

[The following leading article appeared in the *British Medical Journal* on 9 March 1957, at p. 571.—*Editor.*]

Just over a year has passed since the then Minister of Health and his retinue trooped in front of the television cameras to announce the scheme for poliomyelitis vaccination in Great Britain.[1] The dream-like stage thus set before the arc lights has proved to be more fitting than seemed possible at the time. The medical profession in general was then in the dark about the precise nature of the vaccine, and remained so until the Medical Research Council was permitted some weeks later to issue some detailed information on its production, constitution, and testing.[2] Meanwhile the Ministry had announced that enough vaccine for 300,000 to 500,000 children would be ready for injection before the end of June.[3] Events proved this figure to be optimistic, for so far, a year later, only 200,000 have been vaccinated, and some thousands of these have received only one injection. Fortunately the poliomyelitis outbreak last summer was a relatively small one. Not only were cases rather few, but as often happens they were patchily distributed. The Medical Research Council had been collecting statistics of reported cases in order to study the efficacy of the vaccine, but before—indeed, long before—the Council could publish an analysis of the figures the then Parliamentary Secretary to the Ministry had mangled them, in an analysis all her own, to the plaudits of a political audience.[4] In December the Ministry announced that supplies of vaccine were expected to be available from the middle of January,[5] but when the time came a batch of 200,000 doses was found to be faulty and had to be scrapped. The first news of this appeared in a daily newspaper[6] as a result of its science reporter's acumen, and the Ministry later issued a statement. Last week the Ministry called a press conference to communicate the melancholy news that 47 vials in the next and latest batch showed an inexplicable change of *p*H towards acidity. The whole batch must therefore be held back for the time being. How many children can be vaccinated before the poliomyelitis season begins this year is at present conjectural.

The Medical Research Council and the manufacturers are naturally taking every precaution against letting defective vaccine reach the public; their standards, and those prescribed by statute, are such that only a faultless product can, so far as present knowledge goes, successfully pass all the tests. These are not only elaborate and time-consuming but make use of materials, such as live monkeys and tissue cultures, whose variability may be sufficient in itself to vitiate a test even though the product being tested is satisfactory. It is therefore impossible for anyone to predict with certainty, on the resources put into the manufacture of this vaccine, that a batch will be ready at any particular time. The manufacturers hope that another lot will be ready in about two to four weeks, but neither they nor anyone else can be blamed if it is not. What is open to censure is a Ministry that presents genial fantasies of the vaccination programme to the general public. Doubt about the scheme may lead to doubt about the product, while doctors have to suffer the ignominy of being unable to satisfy their patients' falsely raised expectations.

1. *British Medical Journal*, 1956, **1**, 220.
2. Ibid., 1956, **1**, 566.
3. Ibid., 1956, **1**, 225.
4. Ibid., 1956, **2**, 929.
5. Ibid., 1956, **2**, 1496.
6. *Daily Express*, 29 January 1957.

• • •

Dr. Hennie Pretorius has joined Dr. Jac. J. Theron in paediatric practice at 215 Lister Buildings, Jeppe Street, Johannesburg. (Telephones: *Rooms*: 22-0614; *Residence*: 41-4769).

• • •

AN INQUIRY FROM GERMANY ABOUT A SOUTH AFRICAN DOCTOR

Dr. Eugen Heun, Herborn (Dillkreis), Burger Landstrasse 12, Germany, would like to get in touch with the South African doctor who visited him before the war in Berlin and whose name he has forgotten. Would the doctor concerned please write to Dr. Heun at the foregoing address.

• • •

Mr. George Dall, M.Ch. (Cape Town) has joined Mr. Arthur J. Helfet in orthopaedic practice in Cape Town. (Telephones: *Rooms*: 3-2409; *Residence*: 69-1915).

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Mr. Irving B. Hexter has received the Gold Heart award of the American Heart Association. Mr. Hexter is a Vice-President of the American Heart Association and is the seventh recipient of this distinguished award which, in his case, recognizes the importance of lay participation in the activities of the American Heart Association.

Mr. Hexter has been responsible for the collection, since 1950, of the sum of $60,000,000, which was contributed by the public towards the work of the Heart Associations throughout the U.S.A. He also instituted Heart Sunday (the Sunday nearest Valentine's day). Contributions by the public during a single hour on Heart Sunday now amount to $6,000,000 a year.

OVERSEAS MEDICAL CONGRESSES 1957

A SCHEDULE PREPARED FOR THE INFORMATION OF MEDICAL PRACTITIONERS BY KLM ROYAL DUTCH AIRLINES

St. Louis, (Missouri) U.S.	May 14—16	International Audiology Congress
London, U.K.	May 14—17	International Cancer Campaign—Symposium on Biochemistry of Cancer
Paris, France	May 20—25	International Office of Epizootics: Conference
Lisbon, Portugal	May 25—26	VII Congress of International Association for Study of the Bronchi
Lisbon, Portugal	June 3—7	X International Hospital Congress
London, U.K.	June 4—9	International Symposium on Circulation of the Blood
Utrecht, Netherlands	June 5—7	V International Congress of Therapeutics
Malmo, Sweden	June 14—16	European Organisationn for Research of Fluorine and Dental Caries Prophylaxis
Toronto, Canada	June 23—29	IX International Congress of Rheumatic Diseases
Wiesbaden, Germany	June 28—July 5	WHO (European Office) — European Conference on Health Education
Oporto, Lisbon, Portugal	June 21	General Assembly of the International Union against the General Diseases and Treponematoses
Helsinki, Finland	July 1—6	XII International Congress of Industrial Medicine
Brussels, Belgium	July 7—14	International Society of Clinical Pathology—Congress
Geneva, Switzerland	July	International Poliomyelitis Congress IV International Meeting
Rome, Italy	July 8—12	IV International Conference on Poliomeylitis
Paris, France	July 9—12	V Conference of the International Society of Geographical Pathology
Merano, Italy	July 14—19	IV Congress of the International Association of Gerontology
Brussels, Belgium	July 15—20	III International Congress of Clinical Pathology
Venice, Italy	July 20—21	International Symposium on Medical-Social Aspects of Senile Nervous Diseases
Brussels, Belgium	July 19	International Congress on Clinical Pathology
Brussels, Belgium	July 20—21	International Congress on Forensic Pathology
Brussels, Belgium	July 21	Meeting of the International League Against Epilepsy
Brussels, Belgium	July 21—28	VI International Neurological Congress
Brussels, Belgium	July 21—29	Symposium Neuroradiologicum
Brussels, Belgium	July 21—29	International Congress of Electroencephalography and Clinical Neurophysiology
Mexico City, Mexico	July 22—26	International Röntgen Exhibition
Perugia, Italy	July 24—29	International Symposium on the Development of Mammary Cancer
Stockholm, Sweden	July 31—August 6	XI International Congress of Dermatology
Lima, Peru	August 5—11	V Pan-American Congress of Pediatrics
Copenhagen	August 11—17	World Federation of Clinical Chemistry—2nd European Congress
Copenhagen, Denmark	August 26—31	European Society of Haematology — Congress
Chicago, U.S.A.	September 8—12	International College of Surgeons: 22nd Annual Congress and Convocation of the United States and Canadian Sections
Barcelona, Spain	September 16—21	International Society of Orthopedic Surgery & Traumatology: VII Congress
Rome, Italy	September 26—27	International Congress of Chemotherapy
Belgrade, Yugoslavia	September 28—October 6	International Committee of Military Medicine & Pharmacy
Bochum, Germany	September	Congress for Surgery
Istanbul, Turkey	September	World Medical Association. XI General Assembly
London, U.K.	September	Congress of the International Union of the Medical Press
Mexico City, Mexico	September	XVII International Congress of Surgery
Mexico City, Mexico	October 20—27	International Society of Surgery XVII Congress
Mexico City, Mexico	October 29—November 2	International Society of Angiology: III International Congress
Honolulu, U.S.A.	November 14—December	Pan-Pacific Surgical Association: VII Congress

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WITWATERSRAND MEDICAL LIBRARY

BOOKS RECEIVED RECENTLY

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* * *

THE NUTRITION SOCIETY OF GREAT BRITAIN

This Society will hold a symposium on *Nutrition of the Very Young* in Queen's College, Dundee, on 21 September 1957.

* * *

Dr. Willem H. Muller, M.B., Ch.B. (Cape Town), M.O. & G. (Cape Town), formerly of the Department of Obstetrics and Gynaecology, University of Cape Town and Groote Schuur Hospital, has commenced practice as an Obstetrician and Gynaecologist at 4 Strathmore House, Boom Street, Klerksdorp. (Telephones: *Consulting Rooms*: 1120; *Residence*: 1720).

* * *

Dr. Willem H. Muller, M.B., Ch.B. (Kaapstad), M.O. & G. (Kaapstad), voorheen van die Departement van Obstetrie en Ginekologie, Universiteit Kaapstad en Groote Schuur Hospitaal, praktiseer nou as 'n Obstetrikus en Ginekoloog te Strathmoregebou 4, Boomstraat, Klerksdorp. (Telefoon: *Spreekkamers*: 1120; *Woning*: 1720).

* * *

Dr. Leonard Sagorin, M.R.C.P. (Edin.), D.C.H. (Eng.), Paediatrician, formerly in practice in Great Britain and Johannesburg, has joined Dr. Frank Walt in practice at 126 Trust Buildings, Gardiner Street, Durban. (Telephones: *Rooms*: 2-7728; *After hours*: 2-9326; *Residence*: 88-8521).

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WELLCOME TRUST

CARLSBERG-WELLCOME TRAVELLING RESEARCH FELLOWSHIPS

The Directors of the Carlsberg Foundation, in Copenhagen, and the Wellcome Trustees, in London, have decided to institute a system of Carlsberg-Wellcome Travelling Research Fellowships, with the object of encouraging friendly co-operation, on an exchange basis, between Danish and British research workers in any branch of the natural sciences which has a bearing upon human and animal medicine.

One Fellowship annually will be awarded to a candidate from the United Kingdom for a year's work in the United Kingdom.

The stipend may range from £800-£1,200 per annum (or the equivalent sums in Danish Kroner) for whole-time research. Travelling and some incidental expenses will be provided in addition.

It is intended that the first appointments shall be made in respect of the academic year beginning in September 1957.

Enquiries from candidates in the United Kingdom should be addressed to the Scientific Secretary of the Wellcome Trust, 52 Queen Anne Street, London, W.1., from whom further particulars may be obtained.

There is no form of application, but candidates should submit a full *curriculum vitae,* together with details of their research proposals and a supporting letter from a senior scientist who is familiar with their work.

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PREPARATIONS AND APPLIANCES

STERISIL VAGINAL GEL

(BRAND OF HEXETIDINE)

Description: *Sterisil* Vaginal Gel is a new broad-spectrum chemotherapeutic agent. *Sterisil* is highly effective against mixed bacterial, trichomonal and monilial infections, and the newly discovered pathogen *Haemophilus vaginalis* (now believed to be the causal organism most frequently responsible for so-called 'nonspecific' vaginitis and leukorrhea). Recent investigations reveal that *Haemophilus vaginalis* vaginitis has a higher incidence than either trichomoniasis or moniliasis.

Composition: *Sterisil* (brand of hexetidine) 0.1% incorporated in a colourless, non-staining vaginal gel.

Action: *Sterisil* is a markedly effective antimicrobial agent with a high affinity for tissue protein. Because of this affinity and because of the fact that it penetrates the vaginal mucosa, *Sterisil* exerts prolonged antiseptic action.

In vitro studies have revealed no resistance or cross-resistance with *Sterisil*. Topical application of therapeutic concentrations produced no signs of local or systemic toxicity. Sensitization has not been reported after repeated patch testing.

Advantages: Excellent clinical results; high tissue affinity; non-toxic and non-sensitizing; convenient (will not leak or stain); simple (fewer applications).

Dosage: One application every other night until a total of 6 has been reached. This treatment may be repeated if necessary. The gel may be used through the menstrual cycle. A mild alkaline douche (other than soap) may be used before application. Soap solutions are contra-indicated since *Sterisil* is inactivated by soap.

Packaging: 1½ oz. tube with 6 disposable applicators. Instructions for use (applicator filling, insertion and disposal) are included with each package.

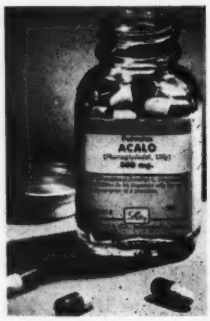
Distributors: Warner Pharmaceuticals (Pty.) Limited, 6-10 Searle Street, Cape Town.

ACALO (PHENAGLYCODOL, LILLY)

A NEW TRANQUILLIZER

Acalo, 2-p-chlorophenyl-3-methyl-2, 3-butanediol, a new chemical synthesized by Eli Lilly & Company, is one of a group of butanediols having a distinct tranquillizing effect.

Pharmacologic studies demonstrate that *Acalo* possesses characteristics common to the interneuronal blocking agents. It represents a new, safe, rapidly effective, mild-acting neuro-sedative.



In clinical practice, *Acalo* combines smooth control of the chronically apprehensive patient with rapid relaxation, freedom from side effects, and simplicity of use.

Acalo quickly allays hyper-excitability, anxiety and tension, without dulling mental acuity or awareness.

Psychological testing has demonstrated that *Acalo* in recommended dosage does not impair speed of fine movements, alertness, attention, visuomotor co-ordination, reaction time or the more complex problem-solving faculties.

Acalo is indicated when a mild tranquillizing or relaxing effect is desirable. It is beneficial in patients who are afflicted with emotional instability, anxiety-tension states or functional disorders.

Acalo has a wide range of application in clinical conditions in which an emotional component is prominent.

The average dose of *Acalo* is 1 pulvule (300 mg.) 3 times daily.

Supplied in pulvules of 300 mg. in packages of 20 and 50.

This product was first introduced in the U.S.A. under the trade name 'Ultran (Phenaglycodol, Lilly)'.

TERTROXIN (GLAXO)

A NEW TREATMENT FOR HYPOMETABOLIC STATES

Tertroxin is the sodium salt of *l*-triiodothyronine. Assessment of its activity in the treatment of myxoedema or by biological test in animals, indicates that 20 to 30 micrograms produce an effect equivalent to that of about 0.1 mg. *l*-thyroxine or about 60 mg. (1 grain) dried thyroid gland.

Tertroxin is probably the ultimately effective form of the thyroid hormone acting directly on the metabolic processes of the cells. It does not have any lengthy latent period before its effects are seen, and on ceasing treatment there is a rapid return to the normal metabolic state.

Tertroxin is completely effective in treating myxoedema, and can be used with greater safety than thyroid in the treatment of the considerable variety of conditions that may arise from hypometabolism and occult hypothyroidism. These include tiredness, ready muscular fatiguability, mental sluggishness, sensi-

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tivity to cold, poor appetite and diminished gastric secretion, constipation, obesity or easy weight gain, infertility and diminished sexual potency, dry skin and brittle hair and nails. Symptoms of the hypometabolic state can be seen at all stages of life. In treating obesity, metabolic stimulation is important and *Tertroxin* is more effective and safer in use than thyroid for this purpose.

Tertroxin is capable of producing the same symptoms (palpitation, headache, etc.) of overdosage as the thyroid hormone, but they disappear rapidly when treatment is stopped or the dosage is reduced.

Packaging: Available in 5 mcgm. and 20 mcgm. tablets. Bottles of 50.

TRILAFON TABLETS

SCHERING CORPORATION

Description: *Trilafon* (perphenazine) is an extremely potent tranquillizing and anti-emetic agent.

Indications: *Trilafon* is indicated in the management of a wide range of mental and emotional disturbances such as anxiety due to both functional and organic disorders, tension, agitation, agitated depression, panic, confusion, restlessness, psychomotor excitement and in post-alcoholic states.

It is highly effective in controlling nausea and vomiting due to various causes such as pregnancy, migraine and tension headaches, gastro-enteritis, cancer, meningeal and psychogenic factors, drug and radiation therapy.

Action: *Trilafon* exhibits specific tranquillizing action in a wide variety of mental and emotional disorders with minimal side effects. Anxiety, tension, apprehension, aggression, psychomotor hyperactivity and fear tend to disappear rapidly, with no dulling of mental activity. Patients become relaxed and quiet with an increased interest in their work and surroundings. Chronic fatigue and despondency based on nervous tension or anxiety are rapidly improved. *Trilafon* increases the patient's capacity to respond to psychotherapy and other therapeutic measures and is therefore of value as adjunct therapy in the treatment of many mental and emotional disturbances encountered in every-day practice.

Trilafon has an extremely potent anti-emetic action and is recommended for the management of nausea and vomiting due to a wide range of conditions.

Advantages: *Trilafon* exhibits extraordinary tranquillizing and behavioural effects without concomitant increases in autonomic, haematological or hepatic side effects. Definite tranquillizing effect has been observed in many patients receiving a total daily dose as low as 16 mg. or less. Side effects such as jaundice, bone marrow depression and narrowing of visual fields associated with other tranquillizing drugs have been notably absent in repeated studies with *Trilafon*. Others, such as blurred vision, nasal congestion and constipation, have been observed only occasionally. Hypnotic effects appear to be minimal, particularly in patients who are permitted to remain active. In studies to date, skin rashes due to the administration of *Trilafon* have not been seen. Other side effects such as nausea or vomiting, urinary frequency and polyphagia appear to be uncommon.

Dosage: Dosage must be adjusted for each individual case. In most patients 4 mg. three or four times daily is effective. The total daily dose ordinarily should not exceed 24 mg. in ambulatory outpatients. Higher levels may be required temporarily in resistant or severely disturbed hospitalized patients. In children over 12 the lower range of the adult dose should be used. Dosage for children under 12 has not been established.

It is important to use the lowest effective dose since extrapyramidal symptoms become more severe and frequent as dosage is increased. Although these symptoms disappear upon withdrawal of the drug or the administration of benztropine methanesulphonate, prolonged administration of doses exceeding 24 mg. daily should be reserved only for patients under constant supervision.

Precautions: Patients receiving *Trilafon* should be chosen with discrimination and should be kept under regular observation. They should be examined regularly for any signs of significant blood changes or other evidence of toxicity.

Trilafon is contra-indicated in comatose or severe depressed conditions, resulting from central nervous system depressants.

The anti-emetic action of *Trilafon* may obscure signs of toxicity due to the overdosage of drugs or the diagnosis of conditions such as brain tumour or intestinal obstruction.

Packings: *Trilafon* Tablets, 2, 4 and 8 mg., bottles of 20 and 100; 16 mg., bottles of 50.

Trilafon Tablets are manufactured in the Union of South Africa for and under the technical supervision of Schering Corporation by Scherag (Pty.) Limited, Johannesburg.

PREPARATE EN TOESTELLE

STERISIL-VAGINA-JEL

('N SOORT HEKSETIDIEN)

Beskrywing: *Sterisil*-vagina-jel is 'n nuwe breëspektrum-chemoterapie-middel. *Sterisil* is hoogs doeltreffend vir die behandeling van gemengde bakteriese, trigomonale en moniliale infeksies, sowel as die pas ontdekte patogeen *Haemophilus vaginalis* (wat, na daar tans gemeen word, die kausale organisme is wat dikwels sogenaamde ‚nie-spesifieke' skedeontsteking en leukorree veroorsaak). Onlangse ondersoek het aan die lig gebring dat skedeontsteking wat deur *Haemophilus vaginalis* veroorsaak word, veel meer dikwels voorkom as òf trigomoniase òf moniliase.

Samestelling: *Sterisil* ('n soort heksetidien) 0.1%, ingelyf by 'n kleurlose, nie-vlekkende vagina-jel.

Effek: *Sterisil* is 'n opvallend doeltreffende mikrobebestrydende middel met 'n hoë affiniteit vir weefselproteïen. Met die oog op hierdie affiniteit en omdat dit die skedeslymvlies binnedring, het *Sterisil* 'n langdurige antiseptiese effek.

In vitro-studies het geen weerstand of kruisweerstand met *Sterisil* aan die lig gebring nie. Plaaslike aanwending van terapeutiese konsentrasies het geen tekens van plaaslike of sistemiese toksisiteit te voorskyn geroep nie. Na herhaalde kol-toetse is geen berigte oor sensitisasie ontvang nie.

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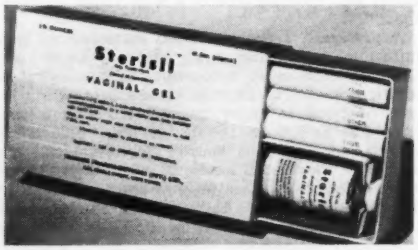

Voordele: Voortreflike kliniese resultate; 'n hoë weefsel-affiniteit; nie-toksies en nie-sensitiserend; gerieflik (sal nie uitlek of vlek nie); eenvoudig (minder aanwendings).

Dosis: Een aanwending al om die ander aand totdat 'n totaal van altesaam 6 bereik is. Hierdie behandeling kan, indien nodig, herhaal word. Die jel kan dwarsdeur die menstruasiekringloop gebruik word. Enige nie-prikkelende alkaliese douche (behalwe seep) kan voor aanwending gebruik word. Seep-oplossings moet nie gebruik word nie, aangesien seep *Sterisil* onaktief maak.

Verpakking: Buisies van 1½ ons, met 6 applikators wat na gebruik vernietig kan word. Gebruiksaanwysings (hoe om die applikator vol te maak, hoe om dit in te steek, en hoe om dit na gebruik te vernietig) word by iedere pakkie ingesluit.

Verspreiders: Warner Pharmaceuticals (Pty.) Limited, Searlestraat, Kaapstad.

ACALO (FENAGLIKODOL, LILLY)

'N NUWE KALMERENDE MIDDEL

Acalo, 2-p-chlorofeniel-3-metiel-2, 3-butanediol, 'n nuwe skeikundige stof wat deur Eli Lilly & Company saamgestel is, is een van 'n groep van butanediols wat 'n beslis kalmerende effek uitoefen.

Farmakologiese studies het bewys dat *Acalo* kenmerke besit wat eie aan die interneuronale versperringsmiddels is. Dit bied u 'n nuwe, veilige, byna oomblik doeltreffende en sagwerkende kalmeermiddel vir die senuwees.

In die kliniese praktyk sorg *Acalo* vir doeltreffende beheer van die kronies vreesbevange pasiënt, gepaard met vinnige ontspanning, vryheid van bykomstige effekte, en eenvoud van gebruik. *Acalo* verlig gou-gou hiper-opgewondenheid, besorgdheid en spanning, sonder om die geesteskerpheid of wakkerheid in enige opsig te verdof.

Psigologiese toetse het aangetoon dat *Acalo*, in die aanbevole dosisse toegedien, nie die snelheid van fyn bewegings, die vlugheid van gedagte, die aandag, die visuomotoriese koördinasie, die reaksietyd, of die meer ingewikkelde probleem-oplossende vermoë belemmer nie.

Acalo word aangedui wanneer 'n sagwerkende kalmerende of ontspannende effek wenslik is. Dit is heilsaam vir pasiënte wat aan emosionele onewewigtigheid, gespanne besorgdheidstoestande of funksionele kwale ly.

Acalo kan gebruik word vir 'n groot verskeidenheid van doeleindes in kliniese toestande waar die emosionele faktor prominent is.

Die gemiddelde dosis *Acalo* is 1 pulvule (300 mg.) 3 maal per dag.

Verkrygbaar in pulvules van 300 mg. in pakkies van 20 en 50.

Hierdie produk is vir die eerste keer in die V.S.A. beskikbaar gestel onder die handelsnaam ‚Ultran (Phenaglycodol, Lilly)'.

TERTROXIN (GLAXO)

'N NUWE BEHANDELING VIR HIPOMETABOLIESE TOESTANDE

Tertroxin is die natriumsout van *l*-triiodotironien. 'n Berekening van die bedrywigheid van hierdie middel by die behandeling van miksedeem, of volgens die biologiese resultate wat met diere behaal is, dui daarop dat 20 tot 30 mikrogram 'n effek het gelykstaande aan dié van ongeveer 0.1 mg. *l*-tiroksien, of ongeveer 60 mg. (1 grein) gedroogde skildklier.

Tertroxin is waarskynlik die uiteindelik doeltreffende vorm van die skildklierhormoon wat regstreeks op die metaboliese prosesse van die selle inwerk. Daar is geen langdurige latente periode voordat die effek daarvan waargeneem kan word nie, en by die staking van die behandeling is daar 'n vinnige terugkeer na die normale metaboliese toestand.

Tertroxin is volkome doeltreffend vir die behandeling van miksedeem, en kan met groter veiligheid as skildklier gebruik word by die behandeling van 'n aansienlike verskeidenheid van toestande wat bes moontlik ten gevolge van hipometabolisme of okkulte -hipotiroïdisme kan ontstaan. Dit sluit in moegheid, maklike spieruitputting, geestelike traagheid, gevoeligheid vir koue, slegte eetlus en verminderde maagafskeidings, hardlywigheid, vetsug of maklike toeneming van gewig, onvrugbaarheid, vermindere geslagtelike bedrywigheid, 'n droë vel en bros hare en naels. Simptome van die hipometaboliese toestand kan op alle stadiums van die lewe waargeneem word. By die behandeling van vetsug is metaboliese stimulasie van belang, en vir hierdie doel is *Tertroxin* nie alleen veiliger nie maar ook doeltreffender as skildklier.

Tertroxin kan dieselfde simptome (hartkloppings, hoofpyn, ens.) as 'n te groot dosis van die skildklierhormoon te voorskyn roep, maar hulle verdwyn byna dadelik as die behandeling gestaak of die dosisse verminder word.

Verpakking: Verkrygbaar in tablette van 5 mkgm. of 20 mkgm. Bottels van 50.

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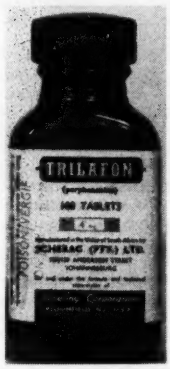
TRILAFON-TABLETTE

SCHERING CORPORATION

Beskrywing: *Trilafon* (perfenasien) is 'n buitengewoon kragtige kalmeer- en brakingsbestrydingsmiddel.

Indikasies: *Trilafon* word aangedui vir die behandeling van 'n groot verskeidenheid van geestes- en emosionele versteurings, soos besorgdheid voortspruitende uit sowel funksionele as organiese ongesteldhede, spanning, verontrusting, verontruste neerslagtigheid, paniekbevangendheid, verwardheid, rusteloosheid, psigomotoriese opgewondenheid en naalkoholiese toestande.

Dit is hoogs doeltreffend vir die bestryding van die mislikheid en braking wat aan verskillende oorsake te wyte is, bv. swangerskap, migraine en gespanne hoofpyn, maag- en dermkatar, kanker, meningo- en psigogeniese faktore, en geneesmiddel- en uitstralingsterapie.



Uitwerking: *Trilafon* het 'n spesifiek kalmerende effek op 'n groot verskeidenheid van geestes- en emosionele ongesteldhede, en die bykomstige reaksies is minimaal. Besorgdheid, spanning, bangheid, aggresiwiteit, psigomotoriese hiperbedrywigheid en vrees het 'n neiging om gou-gou te verdwyn, sonder enige beneweling van die geesteswakkerheid. Pasiënte ontspan en word gekalmeer, en stel groter belang in hul werk en omgewing. Chroniese uitputting en neerslagtigheid voortspruitende uit senuweespanning of besorgdheid word vinnig verban. *Trilafon* verhoog die pasiënt se vermoë om op psigoterapie en ander terapeutiese metodes te reageer, en is derhalwe van waarde as aanvullende terapie by die behandeling van enigeen van die geestes- en emosionele versteurings wat in die alledaagse praktyk teëgekom word.

Trilafon het 'n besonder kragtige brakingbestrydingseffek en word aanbeveel vir die behandeling van die mislikheid en braking wat uit 'n groot verskeidenheid van toestande voortspruit.

Voordele: *Trilafon* oefen 'n merkwaardig kalmerende en gedragseffek uit, sonder meegaande vermeerdering van die bykomstige outonomiese, hematologiese of lewerreaksies. 'n Definitiewe kalmerende uitwerking is waargeneem by baie pasiënte wat 'n totale daaglikse dosis van so min soos 16 mg.—of selfs minder—ontvang het. Bykomstige effekte soos geelsug, beenmurg-depressie en die vernouing van gesigsveld wat met ander kalmerende middels geassosieer word, was opvallend afwesig nadat herhaalde proefnemings met *Trilafon* gedoen is. Ander bykomstige effekte, soos 'n onduidelike gesigsvermoë, verstopping van die neus, en hardlywigheid, is slegs af en toe waargeneem. Dit skyn asof die hipnotiese effek minimaal is, veral by pasiënte wat toegelaat word om aktief te wees. In die proefnemings wat tot dusver gedoen is, is 'n huiduitslag ten gevolge van die gebruik van *Trilafon* nie waargeneem nie. Ander bykomstige effekte soos mislikheid of braking, herhaalde waterlating en polifagie skyn buitengewoon te wees.

Dosis: Die dosis moet by iedere indiwiduele geval aangepas word. Vir die meeste pasiënte is 4 mg. drie of vier maal per dag voldoende. In gewone omstandighede behoort die totale daaglikse dosis nie 24 mg. te oorskry by pasiënte wat in staat is om rond te loop nie. Groter hoeveelhede sal miskien tydelik nodig wees vir pasiënte wat weerstand bied, of vir ernstig versteurde pasiënte wat die bed moet hou. In die geval van kinders bo 12 jaar moet die onderste perke van die dosis vir volwassenes voorgeskryf word. Die dosis vir kinders onder 12 is nog nie vasgestel nie.

Dit is van belang om die laagste doeltreffende dosis voor te skryf, aangesien ekstrapiramidale simptome ernstiger word en meer herhaaldelik voorkom namate die dosis vermeerder word. Hoewel hierdie simptome na onttreking van die middel of die toediening van benstropienmetaansulfonaat verdwyn moet die langdurige toediening van dosisse wat 24 mg. per dag oorskry, voorbehou word slegs vir pasiënte wat onder gedurige toesig staan.

Voorsorgsmaatreëls: Die pasiënte vir wie *Trilafon* voorgeskryf word, moet met oordeelkundigheid gekies word, en hulle moet onder gereelde toesig gehou word. Hulle moet by gereelde tussenpose ondersoek word vir enige tekens van betekenisvolle bloedveranderings of ander bewyse van toksisiteit.

Trilafon moet nie voorgeskryf word in gevalle waar die pasiënt in 'n bewustelose of ernstig terneergedrukte toestand ten gevolge van die gebruik van 'n stilmiddel vir die sentrale senuweestelsel verkeer nie.

Die brakingbestrydingseffek van *Trilafon* bedek miskien die tekens van toksisiteit voortspruitende uit te groot dosisse geneesmiddels, of die diagnose van toestande soos 'n breingewas of ingewandsversperring.

Verpakking: *Trilafon*-tablette, 2, 4 en 8 mg., bottels van 20 en 100; 16 mg., bottels van 50.

Trilafon-tablette word in die Unie van Suid-Afrika voorberei vir en onder die tegniese toesig van die Schering Corporation, deur Scherag (Pty.) Limited, Johannesburg.

BOOK REVIEW

DRUGS AND ADDICTION

Expert Committee on Addiction-Producing Drugs, Seventh Report. World Health Organization: Technical Reports Series, 1957, No. 116. 15 pages. Price: 1s. 9d.

In the seventh report of the *WHO Expert Committee on Addiction-Producing Drugs* it is recommended that the following morphine-like synthetic substances of pethidine type be considered addiction-producing drugs and therefore subjected to the relevant international control: 1-[2-(p-aminophenyl)-ethyl]-4-phenylpiperidine-4-carboxylic acid ethyl ester and α-1-methyl-3-ethyl-4-phenyl-4-propionoxy-piperidine.

The report also deals with several matters of general interest. *Inter alia*, the Committee suggested

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that WHO should study the possibility of organizing, as an adjunct to the technical assistance for narcotics control, symposia or seminars on various problems of drug addiction and addiction-producing drugs. In addition, the Committee was of the opinion that the time was ripe for emphasizing again the distinction between addiction and habit, and approved the definition of certain characteristics of drug habituation.

The abuse of amphetamines is still a serious problem, even in Japan, where the position has improved. Consequently, governments should provide adequate measures of control to prevent any abusive use of such substances.

Because the situation concerning the abuse of barbiturates has not ameliorated, the Committee was of the opinion that control measures at the national level are necessary.

Finally, the attention of the Committee was drawn to the excessive consumption of drugs known as 'tranquillizers' and 'ataraxics'. It is considered that these substances are potentially habit-forming; for this reason their use should be subjected to the same control measures as that of the barbiturates.

CORRESPONDENCE

PENICILLIN REACTIONS AND POLIOMYELITIS VACCINE

To the Editor: In connexion with penicillin reactions following poliomyelitis vaccine, there occurs a major difference of opinion in two journals, the *South African Medical Journal*, 30 March 1957 (Vol. 31, No. 13, p. 319), and *Medical Proceedings*, 30 March 1957 (Vol. 3, No. 7, p. 140) which to my mind, is very important.

In the *South African Medical Journal* the statement reads: 'The amount of antibiotic added is, however, very small, and it is claimed that it is destroyed in the processing of the vaccine. Thus no traces of penicillin has (*sic*) been found by the most sensitive tests in the finished vaccine. There thus would appear to be little danger of a serious penicillin reaction following upon the use of South African or other poliomyelitis vaccine'.

In *Medical Proceedings* we read: 'We drew attention to the penicillin contained in the South African vaccine (or in any other vaccine for that matter) in discussing the problem of the increasing number of penicillin reactions and deaths in South Africa. We stated: "Some routine preventive step has become necessary, because it can be expected that the incidence of penicillin reactions (including deaths) will increase . . . it is known that the South African vaccine contains an appreciable number of units of penicillin per c.c. . . . every susceptible child in the population will become sensitized to penicillin, with the possibility of a serious reaction, when the antibiotic is used subsequently in therapeutic amounts".'

Surely these two statements are in complete conflict with each other, and one would expect further elucidation.

Dr. J. P. de Villiers, M.O.H. of the Cape Divisional Council states that no poliomyelitis reactions were reported in the 15,000 children who received poliomyelitis vaccine, but what has happened to some of these children (surely there must be quite a number) who have since received penicillin therapy?

Ben Cheifitz.

Barclays Bank Building,
Adderley Street,
Cape Town.

[In our Editorial of 30 March 1957, p. 140, we pointed out that a warning (under the heading *Contra-Indications*) is uttered against penicillin reactions, as a result of using the poliomyelitis vaccine manufactured in South Africa, in the leaflet accompanying as recent a batch of the vaccine as that issued by the South African Poliomyelitis Research Foundation on 13 March 1957. The warning is against administering the vaccine to persons known to be sensitive to penicillin.

This same leaflet also carries the unequivocal statement that the South African poliomyelitis vaccine contains 100 units of penicillin per c.c.

In the *South African Medical Journal* of 1 October 1955, p. 947, Dr. M. Shapiro pointed out that: '. . . the potential hazard from mass inoculation with penicillin of an entire generation of children (as distinct from the relatively few who receive penicillin for therapeutic purposes) creates a potential hazard for every child capable of being sensitized. As sensitization depends not on the quantity of the allergen but on the susceptibility of the individual, and as it is trite medicine that this may follow parenteral injection of minute amounts of the allergen, it becomes difficult to understand Dr. Gear's unsupported allegation that "it is likely that many more children will be sensitized by therapeutic use of penicillin than from poliomyelitis vaccine". Ringing the changes on the available antibiotics for future batches of vaccine does not eliminate the hazard of penicillin sensitization to those at present being inoculated. My point was that sensitization to penicillin by the vaccine would place at risk those susceptible individuals who might subsequently require penicillin in *therapeutic* doses for the treatment of other diseases. The increasing hazard of penicillin sensitization is dramatically illustrated by the report of yet another case in the column which appears cheek by jowl with Dr. Gear's letter'.

The contentions in Dr. M. Shapiro's statement have not been controverted or replied to.

There is no way, at present, of collecting adequate data about the susceptible children who may have been sensitized by penicillin contained in the South African poliomyelitis vaccine and who have subsequently received therapeutic injections of the antibiotic, desirable as it may be to have this information. The statement by Dr. de Villiers that no *poliomyelitis* reactions were reported in the 15,000 children who received the vaccine is, of course, totally irrelevant to the issue under consideration. But in the very next sentence in the passage from which our correspondent has quoted Dr. de Villiers' observations, Dr. R. Turner admits (albeit ungrammatically) that the possibility that a sensitivity reaction may follow the inoculation of poliomyelitis vaccine into a sensitized child, cannot be entirely excluded. This admission only makes sense on the basis that the vaccine does, in fact, contain penicillin.

Our purpose in drawing attention to penicillin reactions was to alert medical practitioners to a very real danger which modern preventive medicine can bring about and to remind them that antihistamines provide a potent weapon against a serious risk.—*Editor.*]

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1. Peele, J.C.: A.M.A. Arch. Otolaryng. 61:450 (April, 1955).

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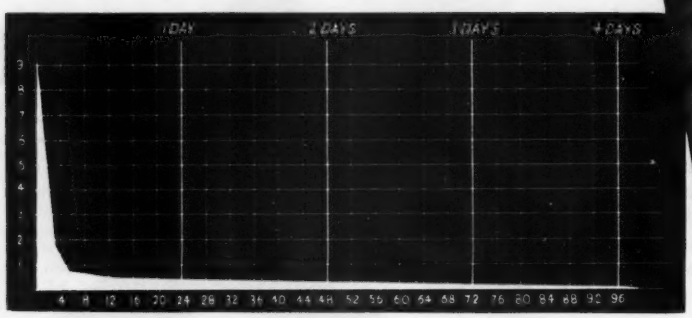

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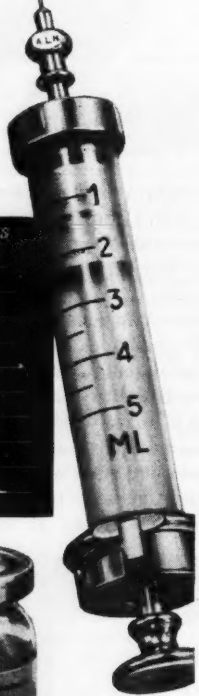

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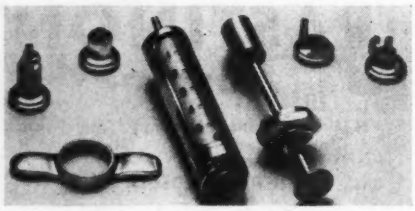

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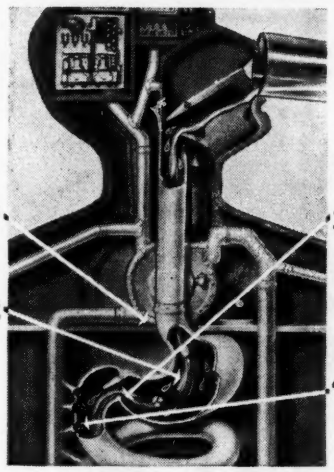

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* Effect of Buffering Agents on Absorption of Acetylsalicylic Acid. J.Am. Pharm.A., Sc.Ed. 39: 21, Jan., 1950.

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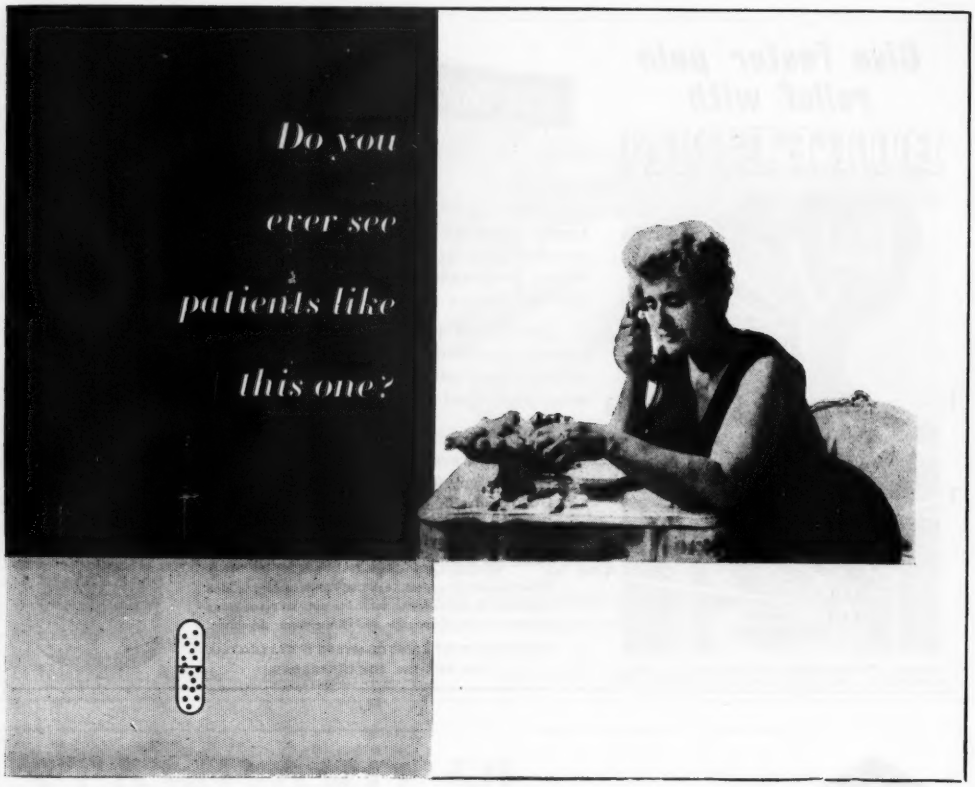

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1. Braceland, F. J.: Texas State J. Med. *51*:287 (June) 1955.
2. Lemere, F.: Northwest Med. *54*:1098 (Oct.) 1955.

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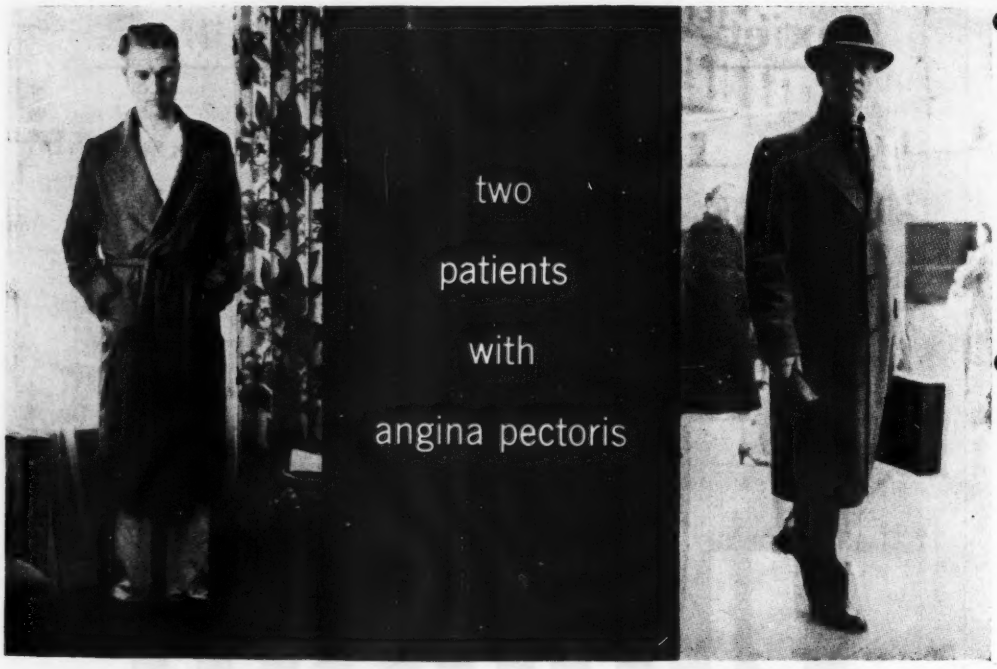

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Usual Dosage: 10 to 20 mg. *before meals* and at bedtime.

References: 1. Rosenburg, H. N., and Michelson, A. L.: Am. J. M. Sc. 230: 254 (Sept.) 1955. 2. Kory, R. C., *et al.*: Am. Heart J. 50: 308 (Aug.) 1955. 3. Winsor, T., and Humphreys P.: Angiology 3: 1 (Feb.) 1953. 4. Plotz, M.: New York State J. Med. 52: 2012 (Aug. 15) 1952. 5. Dailheu-Geoffroy, P.: L'Ouest-Medical, vol. 3 (July) 1950.

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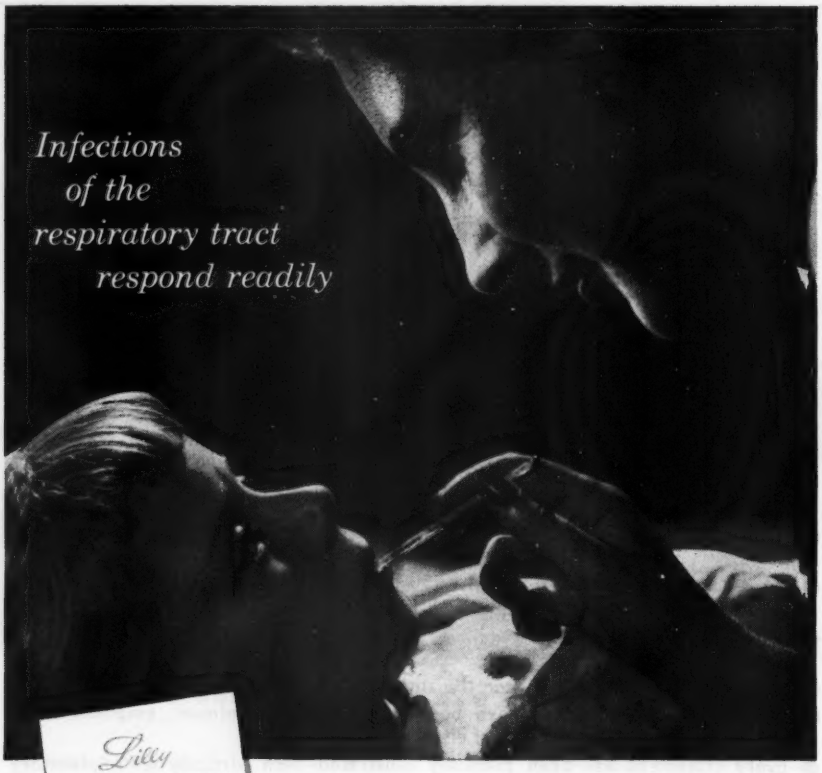

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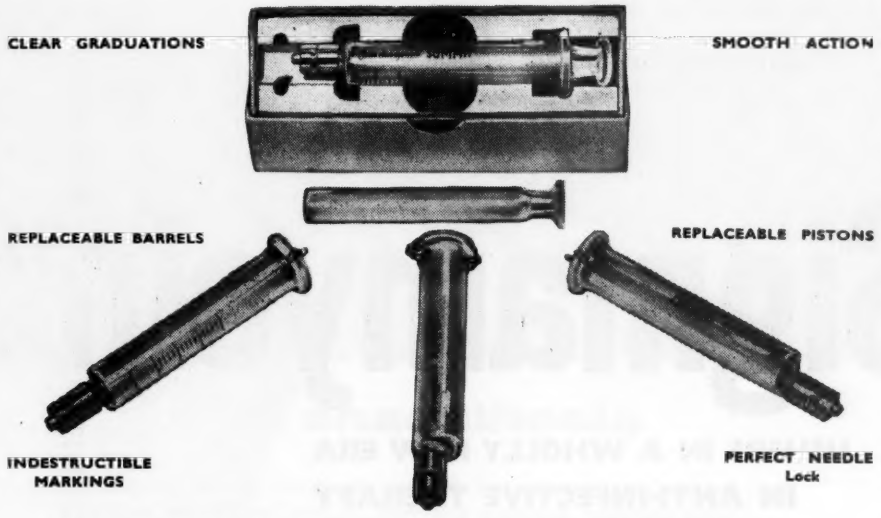

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Ref. SOBIN et al., Antibiotics Annual 1954-55 p. 827.

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Ref. Personal communication presented at Antibiotic Symposium 1956.

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Ref. ENGLISH et al., Antibiotics and Chemotherapy VI: 511. August 1956.

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Ref. ROYES et al., Antibiotics and Chemotherapy VI: 450. July 1956.

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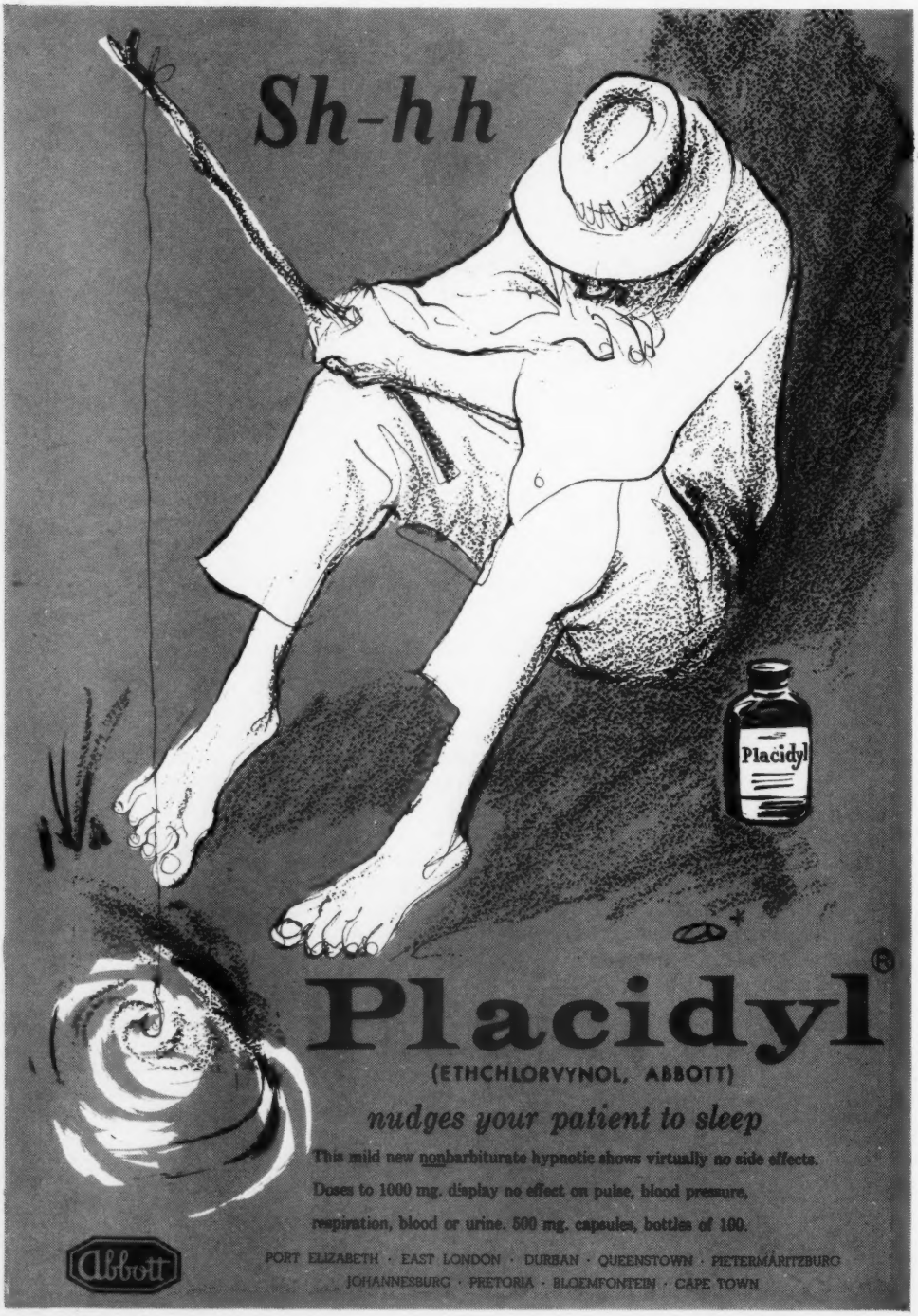

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